**PATENT** 

**DOCKET NO.: PHOE-0057** 

**Application No.:** 09/504,280

Office Action Dated: July 14, 2003

This listing of claims will replace all prior versions, and listings, of claims in the application.

**Listing of Claims:** 

(currently amended) Modified TNF, comprising TNF covalently bound to between 1.

about five and twelve PEG molecules having an approximate weight average molecular

weight in the range of  $\frac{10,000}{15,000}$  15,000 to about 40,000.

2. (currently amended) The modified TNF of Claim 1 wherein said PEG is covalently

bound to primary amine groups on said TNF through a biocompatible linker and where said

PEG has an approximate weight average molecular weight in the range of about 20,000 to

about 30,000.

3. (previously presented) The modified TNF of claim 24 wherein said linker is selected

from the group consisting of succinimidyl succinate, succinimidyl proprionate, and N-

hydroxy succinimidyl.

4. (original) The modified TNF of Claim 2 wherein said linker is selected from the

group consisting of succinimidyl succinate, succinimidyl proprionate, and N-hydroxy

succinimidyl.

5. (original) The modified TNF of Claim 1 wherein said TNF is TNF- $\alpha$ .

6. (original) The modified TNF of Claim 1 wherein said TNF is isolated human TNF. DOCKET NO.: PHOE-0057 PATENT

Application No.: 09/504,280

Office Action Dated: July 14, 2003

7. (original) The modified TNF of Claim 1 wherein said TNF is recombinant human

TNF.

8. (original) The modified TNF of Claim 1 wherein said TNF is human TNF mutated by

deleting amino acids 1-9 of the mature TNF protein.

9-13. (canceled)

14. (currently amended) A method of enhancing the circulating half life of TNF while

reducing its toxicity comprising modifying said TNF by covalently bonding to it between

about five and twelve PEG molecules having an approximate weight average molecular

weight in the range of 10,000 15,000 to about 40,000.

15. (currently amended) The method of Claim 14 in which said PEG is covalently bound

to primary amine groups on said TNF through a biocompatible linker and where said PEG

has an approximate weight average molecular weight in the range of about 20,000 to about

30,000.

16. (currently amended) A method of enhancing the tumoricidal activity of TNF

comprising modifying said TNF by covalently bonding to it between about five and twelve

PEG molecules each molecule having an approximate molecular weight of 20,000 to 30,000.

Page 3 of 14

**PATENT** 

**DOCKET NO.:** PHOE-0057 **Application No.:** 09/504,280

Office Action Dated: July 14, 2003

17. (currently amended) The method of Claim 16 in which said PEG is covalently bound

to primary amine groups on said TNF through a biocompatible linker and where said PEG

has an approximate weight average molecular weight in the range of about 20,000 to about

30,000.

18-23. (canceled)

24. (previously presented) The modified TNF of claim 1 wherein said PEG is covalently

bound to primary amine groups on said TNF through a biocompatible linker.